

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

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SEP 23 2002

Food and Drug Administration Center for Biologics Evaluation and Research 1401 Rockville Pike Rockville MD 20852-1448

By Certified Mail – Return Receipt Requested And by Facsimile Transmission

CBER - 02- 015

Warning Letter

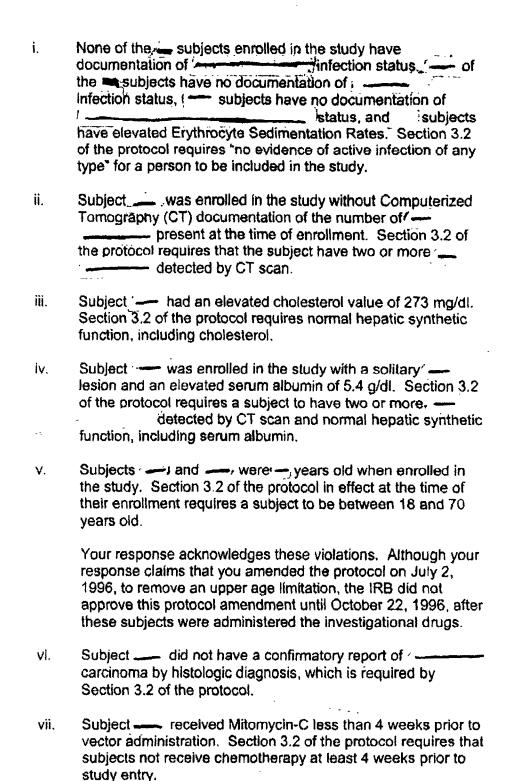
Ronald G. Crystal, M.D. 515 East 71st Street New York City, New York 10021

Dear Dr. Crystal:

investigator with the	The inspection was conducted under the FDA's ch Monitoring Program that includes inspections designed to review the ficlinical research involving investigational drugs. A Form FDA 483, List	
conduct of clinical re	ring Program that includes inspections designed to review the	
conclusion of the in	spection.	

We have reviewed your written response dated May 2, 2002, addressed to the FDA New York District Office, to the Form FDA 483, and have determined that you violated regulations governing the proper conduct of clinical studies involving investigational new drugs, as published in Title 21, Code of Federal Regulations (CFR) Parts 50 and 312 (available at http://www.access.gpo.gov/nara/cfr/index.html). The applicable provisions of the CFR are cited for each violation.

- 1. You failed to ensure that the investigation was conducted according to the investigational plan (protocol). [21 CFR § 312.60].
 - A. You failed to follow the protocol by enrolling subjects who did not satisfy the eligibility criteria. You enrolled a total of subjects in the study. None of the subjects met the criteria for inclusion. You administered the investigational product to subjects who should have been excluded, as described below.

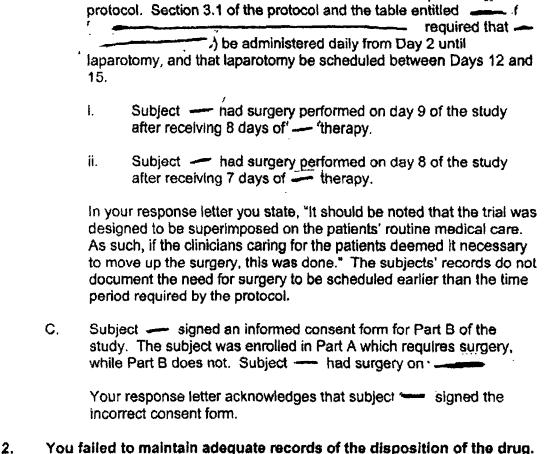


[21 CFR § 312.62(a)].

B.

We note that you authored and signed a separate Memorandum to the File dated March 15, 2002 for each of the — enrolled subjects. In each Memorandum, you acknowledge the above issues relating to eligibility criteria for each subject. While we recognize that you documented these deficiencies, we note that these memoranda were not written until March 15, 2002, after you were contacted by the FDA in February 2002 to schedule this inspection.

You falled to follow the time intervals for treatments specified in the



In your response letter, you acknowledge the lack of drug accountability records retained during the course of this study, and state your commitment to maintaining these records in the future.

You failed to maintain adequate records of the disposition of the test article

administration to subjects, and the amount of stock remaining.

including quantity received, quantity used, lot number,

3. You failed to prepare and maintain adequate and accurate case histories. [21 CFR § 312.62(b)].

A signed informed consent form could not be located for Subject -.

Your response letter acknowledges this violation.

This letter is not intended to be an all-inclusive list of deficiencies with your clinical study. It is your responsibility as the clinical investigator to ensure adherence to each requirement of the law and applicable regulations and to protect the rights, safety, and welfare of subjects under your care.

Your response letter describes several corrective actions you have implemented to correct these violations and to ensure that all applicable regulations and guidelines are followed for future studies. In addition, your response letter describes changes at the Institute of Genetic Medicine (IGM). The IGM has instituted new Standard Operating Procedures (SOP's) for clinical trials and hired additional personnel.

This Warning Letter is issued to you because of the serious nature of the observations noted at the time of the FDA inspection. Please be advised that the failure to effectively put into practice the corrective actions you have described in your response letter, and/or the commission of other violations, may warrant the initiation of enforcement actions without further notice. These actions could include initiation of clinical investigator disqualification proceedings, which may render a clinical investigator ineligible to receive investigational new drugs, and/or injunction.

In light of the corrective actions that you described in your response letter, no response to this letter is required. However, if you do choose to respond to this letter, please send your written response to:

Christine Drabick
Division of Inspections and Surveillance (HFM-664)
Office of Compliance and Biologics Quality
Center for Biologics Evaluation and Research
Food and Drug Administration
1401 Rockville Pike, Suite 200N
Rockville, MD 20852-1448
Telephone: (301) 827-6221

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We also request that you send a copy of any response to the FDA District Office listed below.

Sincerely,

Steven A. Masiello

Director

Office of Compliance and Biologics Quality

Center for Biologics Evaluation and

Research

cc: Jerome G. Woyshner, Director Food and Drug Administration 158-15 Liberty Avenue Jamaica, New York 11433

> David A. Behrman, DMD, Chair Institutional Review Board New York Hospital-Comell Medical Center 1300 York Avenue New York, New York 10021